

Research article

# Sodium Pyrophosphate: A Novel and Efficient Catalyst for Sulfa-Michael additions

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## Abstract

The Sodium Pyrophosphate is a new basic catalyst for Sulfa-Michael addition between chalcone derivatives and aliphatic or aromatic thiols with high yields in few minutes and mild reaction conditions. By-products of usual undesirable reactions in Michael addition such as 1.2-addition, bis-addition and polymerisation are not observed. The yields obtained are good to excellent. **Copyright © AJBCPS, all rights reserved.**

**Keywords:** Michael addition, Sodium Pyrophosphate, Heterogeneous catalysis, thiols, Chalcones.

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## 1. Introduction

Life itself is the uncontested, ever-present proof of the importance of sulfur-containing and sulfur-based compounds [1]. Many biochemical processes in nature involve sulfur, be it in organic or inorganic form [2]. From a purely synthetic point of view, the words variety and richness describe best the chemistry of sulfur [3]. Among the various methods for the generation of carbon-sulfur bonds [4], the Michael addition (or 1,4-addition) reaction is a straightforward route [5]. This transformation takes advantage of the mild nucleophilicity of sulfur nucleophiles in general and of the thiophenolate anion in particular. Its propensity to react with activated double bonds provides thioethers as products. Diversity of the reaction partners, flexibility of the Michael adduct (that can be used as such or easily cleaved, reduced or oxidized) [6].

Traditionally, the Michael addition of mercaptans to  $\alpha,\beta$ -unsaturated carbonyl compounds is catalyzed by strong bases such as alkali metal alkoxides [7], hydroxides [8], and amines [9]. However the use of either strongly acidic or basic conditions [10] frequently leads to the formation of undesirable side products owing to competing reactions, such as polymerization, self-condensation and rearrangements.

Nevertheless, advantages of the heterogeneous synthesis are very interesting; reactions take place in simple and mild conditions [11]. The products obtained are generally pure and separated easily. Thus, numerous organic reactions have been carried out in solid/liquid heterogeneous media. So, several types of catalysts or solid supports have been studied, we can mention hydrotalcite [12], alumina [13], montmorillonite [14], zeolites [15], silica [16], animal bone meal [17] and solid state phosphate [18].

In continuation of our ongoing program to develop a heterogeneous catalysis, we describe in this paper, the Sulfa-Michael addition between chalcone derivatives and aliphatic or aromatic thiols catalyzed by Sodium Pyrophosphate.

## 2. Materials and Method

### 2.1. Chemicals and Instrumentations.

All commercial reagents and solvents were used without further purification. X-ray diffraction (XRD) patterns of the catalysts were obtained on a D500 diffractometer using Cu-K $\alpha$  radiation. NMR spectra were recorded on a Bruker ARX 300 spectrometer. FTIR spectra were recorded on an ATI Mattson-Genesis Series spectrophotometer using the KBr disc method.

### 2.2. Preparation and Characterization of Catalyst.

The anhydrous  $\text{Na}_4\text{P}_2\text{O}_7$  [19] was prepared by dehydration of the commercial sodium pyrophosphate decahydrate [20]  $\text{Na}_4\text{P}_2\text{O}_7 \cdot 10\text{H}_2\text{O}$  at  $600^\circ\text{C}$ . This dehydration has been carried out progressively by steps of  $100^\circ\text{C}$ . Then this powder has been desiccated under vacuum. The identity of  $\text{Na}_4\text{P}_2\text{O}_7$  powder was confirmed by X-ray diffraction (Figure 1). The X-ray profiles recorded on  $\text{Na}_4\text{P}_2\text{O}_7$  show a good agreement with the ICSD 10370 file of this product [21].

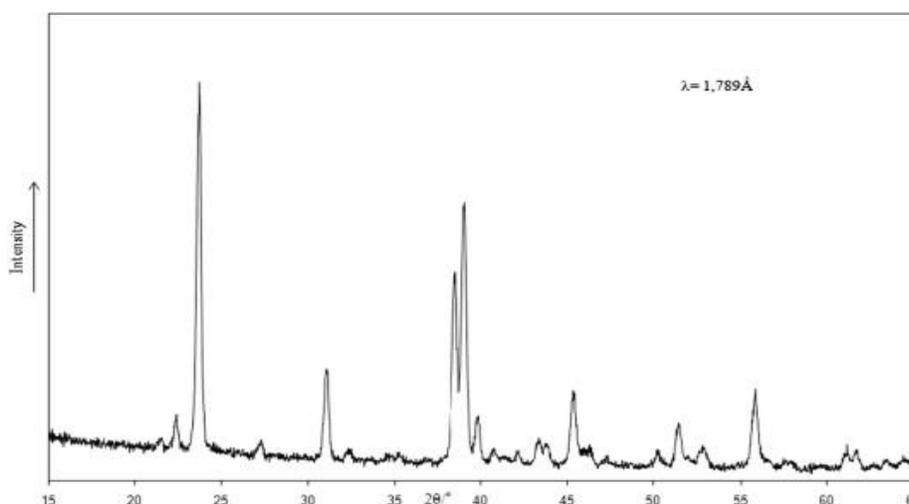


Figure 1: Diffractogram of  $\text{Na}_4\text{P}_2\text{O}_7$ .

The powder was dried for 2 hours at 100°C before use in order to eliminate possible water molecules adsorbed on the surface of the sample which may affect catalytic activity.

### 2.3. Catalytic Tests.

The general procedure is as follows: To a flask containing an equimolar mixture (1 mmol) of Michael acceptors **1** and Michael donors **2** in methanol (1.5 ml), Na<sub>4</sub>P<sub>2</sub>O<sub>7</sub> (0.1 g) was added and the mixture was stirred at room temperature until completion of the reaction, as monitored by thin layer chromatography.

The catalyst was filtered, washed with dichloromethane and the filtrate was concentrated under reduced pressure. The crude product was purified by recrystallization. The product was analyzed by <sup>1</sup>H, <sup>13</sup>C NMR and IR spectrometry.

## 3. Results and Discussion

First of all, we have studied the use of the synthetic diphosphate Na<sub>4</sub>P<sub>2</sub>O<sub>7</sub> for catalytic Michael reaction. Conjugate addition between chalcone and thiophenol was chosen to optimize the reaction conditions. Thus, the synthesis of product **3a** using 1 mmol of substrates, 0.1g of catalyst and 1.5ml of various solvents has been tested. After a time of 10 min the best yields were obtained in methanol (93%) and ethanol (72%). No reaction was observed in the presence of Hexane, Dichloromethane, Ethyl acetate, Tetrahydrofuran and 1,4-Dioxane, only the starting material was isolated. This result confirms the crucial role played by the solvent used to carry out the reaction. Thus, methanol was chosen as a solvent for further study. Thereafter, we examined the weight effect of the catalyst in this reaction. The yield of product **3a** increased effectively as the catalyst weight increased to 0.1-0.3 g and increased slightly above 0.3g of catalyst. Thus, we have chosen a weight of 0.1g catalyst for further study. As a result of the optimization of Michael addition, we found that increased yields were observed when the reaction was conducted in 1.5ml of methanol using 0.1g of the synthetic diphosphate Na<sub>4</sub>P<sub>2</sub>O<sub>7</sub>. To determine the scope and limitation of this reaction, the optimum condensations were applied to other substrates as shown in table **1**.

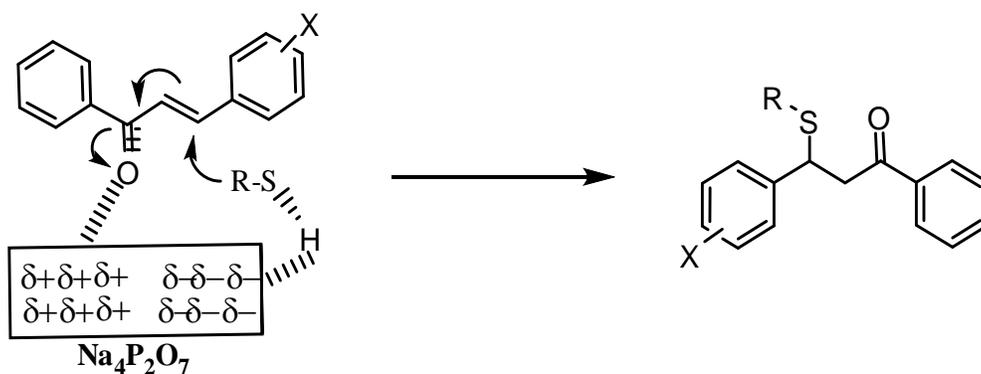
**Table 1:** Synthesis of sulfanyl derivatives catalyzed by Sodium Pyrophosphate.

Products	R	X	Yield % (time/min)
3a	H	-Ph	93 (10)
3b	H	-2-NH <sub>2</sub> -Ph	91 (02)
3c	H	-CH <sub>2</sub> -CO <sub>2</sub> -Et	74 (25)
3d	<i>p</i> -NO <sub>2</sub>	-Ph	93 (02)
3e	<i>p</i> -NO <sub>2</sub>	-2-NH <sub>2</sub> -Ph	94 (01)
3f	<i>p</i> -NO <sub>2</sub>	-CH <sub>2</sub> -CO <sub>2</sub> -Et	94 (25)
3g	<i>p</i> -Cl	-Ph	97 (02)
3h	<i>p</i> -Cl	-2-NH <sub>2</sub> -Ph	91 (01)
3i	<i>p</i> -Cl	-CH <sub>2</sub> -CO <sub>2</sub> -Et	85 (25)
3j	<i>p</i> -Me	-Ph	92 (30)
3k	<i>p</i> -Me	-2-NH <sub>2</sub> -Ph	92 (03)
3l	<i>p</i> -Me	-CH <sub>2</sub> -CO <sub>2</sub> -Et	67 (25)
3m	<i>p</i> -OMe	-Ph	93 (80)
3n	<i>p</i> -OMe	-2-NH <sub>2</sub> -Ph	93 (05)
3o	<i>p</i> -OMe	-CH <sub>2</sub> -CO <sub>2</sub> -Et	53 (25)

Several structurally varying donors such as thiophenol, 2-aminothiophenol and ethyl thioglycolate underwent clean and remarkably catalyst Michael addition with a variety of acceptors including simple and substituted chalcones.

The products of undesirable side reactions resulting from 1,2 addition, polymerization and bis-addition are not observed. The yields obtained with synthetic diphosphate  $\text{Na}_4\text{P}_2\text{O}_7$  are very high and exceed 91 % in short reaction time, except for the sulfanyl products (**3c**, **3i**, **3l**, and **3o**). In this case, the low reactivity observed may be due to low nucleophilicity of ethyl thioglycolate. For sulfanyl products (**3o**, **3l**), the longer reaction time observed may be to the presence an electron-donor. Our results are generally equal or better than those of the literature. For example, in the synthesis of sulfanyl product **3i**, the yield(time) obtained with the synthetic diphosphate  $\text{Na}_4\text{P}_2\text{O}_7$  is equivalent to that of natural phosphate (86%(20 min)) [22], and greater to that of synthetic diphosphate  $\text{Na}_2\text{CaP}_2\text{O}_7$  (63%(40 min)) [23], Fluorapatite (82%(60 min)) [24], but smaller with that of Hydroxyapatite [25].

Thus, we estimate that the surface of the synthetic diphosphate  $\text{Na}_4\text{P}_2\text{O}_7$  presents certainly multicatalytic active sites (Figure 2).



**Figure 2:** Sulfa Michael addition catalyzed by  $\text{Na}_4\text{P}_2\text{O}_7$ .

The basic sites (oxygen of  $\text{P}_2\text{O}_7$  group) enhance the donors nucleophilicity. The acidic sites ( $\text{Na}^+$  and phosphorus  $\text{P}_2\text{O}_7$  group) probably increase the enone moiety polarization. Consequently, the carbon-sulfur bond formation is accelerated and the sulfanyl product is obtained by the transfer of proton.

## Conclusion

In summary, we believe that these new supported reagents for effecting carbon-sulphur bond formation represent an important breakthrough in the development of solid catalysts. The high reactivity and regioselectivity of sodium pyrophosphate coupled with their ease of use and reduced environmental problems makes them attractive alternatives to homogeneous basic reagents.

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